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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/842,364 | 04/25/2001 | Frances Yen-Potin | GENSET.50CP2C | 6570 |

23557 7590 01/31/2003

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EXAMINER

GOLDBERG, JEANINE ANNE

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1634

DATE MAILED: 01/31/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/842,364

Applicant(s)

YEN-POTIN ET AL.

Examiner

Jeanine A Goldberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 5-14 and 16-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14, 17.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed November 4, 2002. Currently, claims 1-17 are pending. Claims 5-15, 17 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election of Group I, Claims 1-4, 15) in Paper No. 11 is acknowledged.

Applicant's response filed November 4, 2002 was not fully responsive because applicant did not select a single biallelic allele as required by the restriction requirement mailed September 27, 2002. On November 13, 2002, the examiner called Frank C. Eisenschenk to ask for a further restriction. The applicant indicated that they would like to pursue the biallelic marker at position 12347 of SEQ ID NO: 1. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-14, 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

The requirement is still deemed proper and is therefore made FINAL.

.Priority

3. This application claims priority to provisional applications 60/113,686, filed December 22, 1998 and 60/141,032, filed June 25, 1999. Neither of these applications teaches an isolated nucleic acid comprising the biallelic marker of T at position 12347 of SEQ ID NO: 1.

Similarly 09/469,09, filed December 21, 1999 and PCT/IB99/02058, filed December 20, 1999 does not disclose a nucleic acid comprising a T at position 12347 of SEQ ID NO: 1.

The application also claims priority to 09/599,362, filed June 21, 2000 which appears to be the first description of a nucleic acid comprising a T at position 12347 of SEQ ID NO: 1. Therefore, the instant claims are awarded the benefit of the June 21, 2000 filing date.

Drawings

4. The drawings are objected by the examiner. The drawings include sequences which are not identified by SEQ ID NO: either in the figure or in the description of the figures. Appropriate correction is required.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the

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list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The specification contains a list of references on pages 151-159.

Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

It is noted that on page 143, lines 20-21, there is no identifier for the sequence listed. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

In an effort to facilitate compact prosecution, this rejection is applied to the claims in the event that the claims are amended to overcome the art rejections below. While it is noted that numerous nucleic acids have been described by the prior art to be encompassed by the instant claims, a narrow embodiment of Applicant's invention is a nucleic acid sequence comprising SEQ ID NO: 1 wherein a T is present at position

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12347. This nucleic acid sequence comprising SEQ ID NO: 1 wherein a T is present at position 12347 lacks utility.

The specification teaches that SEQ ID NO: 1 is a partial genomic sequence from chromosome 11. The specification teaches that AA4RP is differentially expressed in obese mice (page 3).

The specification asserts that the biallelic markers of position 12347 of SEQ ID NO: 1 may be used to determine where an individual is at risk of developing a disease involving lipid metabolism and/or a liver related disorder at a later date or whether the individual suffers from a lipid metabolism related disorder and/or a liver related disorder as a result of a mutation in the AA4RP gene (page 5). The specification teaches analyzing and identification of new biallelic markers (page 142). The donors were unrelated and healthy.

The specification fails to provide any specific or substantial utility for the polymorphic nucleic acids of SEQ ID NO: 1 wherein at position 12347 of SEQ ID NO: 1, there is a T nucleotide. The specification has asserted that the detection of the polymorphic nucleic acids would facilitate the determination of an individual's risk of developing a disease involving lipid metabolism and/or a liver related disorder at a later date or whether the individual suffers from a lipid metabolism related disorder and/or a liver related disorder as a result of a mutation in the AA4RP gene (page 5). The specification fails to provide any association between the polymorphism at position 12347 of SEQ ID NO: 1 and any disease. Therefore, the skilled artisan would have to perform additional experimentation to confirm a real world use for the polymorphic

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nucleic acid. As provided by Lee, "up to 20% of SNPs might be private SNPs found only in a small number of people". Moreover, Venter suggested that "a large fraction of the current SNP dataset will not be very useful, estimating that of the 2.3 million human SNPs, only 2,000 change an amino acid." It is noted that the instant change in sequence does not appear to change the amino acid sequence. Therefore, it is unclear what affect the change in nucleotide sequence has, if any, in lipid metabolism as suggested by the specification.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4, are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In an effort to facilitate compact prosecution, this rejection is applied to the claims in the event that the claims are amended to overcome the art rejections below. While it is noted that numerous nucleic acids have been described by the prior art to be encompassed by the instant claims, a narrow embodiment of Applicant's invention is a nucleic acid sequence comprising SEQ ID NO: 1 wherein a T is present at position

12347. This nucleic acid sequence comprising SEQ ID NO: 1 wherein a T is present at position 12347 lacks utility.

The claims are drawn to a nucleic acid molecule comprising a T at position 12347 of SEQ ID NO: 1.

The specification teaches that SEQ ID NO: 1 is a partial genomic sequence from chromosome 11. The specification teaches that AA4RP is differentially expressed in obese mice (page 3).

The specification asserts that the biallelic markers of position 12347 of SEQ ID NO: 1 may be used to determine where an individual is at risk of developing a disease involving lipid metabolism and/or a liver related disorder at a later date or whether the individual suffers from a lipid metabolism related disorder and/or a liver related disorder as a result of a mutation in the AA4RP gene (page 5). The specification teaches analyzing and identification of new biallelic markers (page 142). The donors were unrelated and healthy.

Neither the specification nor the art provide the skilled artisan enough guidance to practice the invention as broadly as claimed. The specification fails to provide any association between the polymorphic nucleic acids of SEQ ID NO: 1 wherein at position 12347 of SEQ ID NO: 1, there is a T nucleotide and any disease or condition. The specification has asserted that the detection of the polymorphic nucleic acids would facilitate the determination of an individual's risk of developing a disease involving lipid metabolism and/or a liver related disorder at a later date or whether the individual suffers from a lipid metabolism related disorder and/or a liver related disorder as a result

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of a mutation in the AA4RP gene (page 5). The specification fails to provide any association between the polymorphism at position 12347 of SEQ ID NO: 1 and any disease. Therefore, the skilled artisan would have to perform undue, unpredictable experimentation to determine how to use for the polymorphic nucleic acid. As provided by Lee, "up to 20% of SNPs might be private SNPs found only in a small number of people". Moreover, Venter suggested that "a large fraction of the current SNP dataset will not be very useful, estimating that of the 2.3 million human SNPs, only 2,000 change an amino acid." It is noted that the instant change in sequence does not appear to change the amino acid sequence. Therefore, it is unclear what affect the change in nucleotide sequence has, if any, in lipid metabolism. While one could conduct additional experimentation to determine whether, e.g., the presence of a T at position 12347 of SEQ ID NO: 1 might be associated with, e.g., lipid metabolism, the outcome of such research can not be predicted, and such further research and experimentation are both unpredictable and undue. The teachings in the specification do not establish that one could actually detect the presence of a T at position 12347 of SEQ ID NO: as an indicator of any disease or condition. Rather the teachings of the specification merely set for the assertion that the detection facilitate the determination of the risk. The specification has not established which allele is associated with what risk, e.g, increased risk or decreased risk. In absence of guidance from the specification, one skill in the art may look to the teachings of the prior art for enablement of the claimed invention. However, the closest prior art does not discuss any variations within a nucleic acid and any association between a disorder. Thus, it is unpredictable whether

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one could successfully use the claimed invention, and given the fact that neither the specification nor the prior art provide evidence of a correlation or association between a T at position 12347 of SEQ ID NO: and any disease or condition, it is further unpredictable as to whether any quantity of experimentation would allow one to practice the claimed invention. Accordingly, it would require undue experimentation for a skilled artisan to use the claimed invention.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any nucleic acid comprising at least 8 contiguous nucleotide of SEQ ID NO: 1, wherein the span includes a AA4RP-related biallelic marker. The claim are also broadly drawn to a nucleic acid encoding at least 6 amino acids from SEQ ID NO: 3.

The specification describes six biallelic alleles from the AA4RP-related nucleic acid (Figure 1, Table 1, page 30). As provided in the specification, SEQ ID NO: 1 is a partial genomic sequence from chromosome 11; SEQ ID NO: 2 contains a cDNA sequence of AA4RP, SEQ ID NO: 3 is the amino acid sequence encoded by the cDNA

of SEQ ID NO: 2; and SQ ID NO: 4 contains an alternative genomic sequence of AA4RP (page 14). The nucleic acid of SEQ ID NO: 1 is 81,001 nucleotides in length.

The specification does not describe any polynucleotide minimally comprising 8 contiguous nucleotides of SEQ ID NO: 1. As provided in the rejections below under 35 U.S.C. 102, nucleic acids minimally comprising 8 nucleotides are prevalent in nucleic acids of cow, AD 17 adenoviral vectors, for example. Additionally, the claims broadly encompass nucleic acids which are from *Staphylococcus epidermidis*, pan troglodytes, *mus musculus*, *ratus norvegicus* and *caenorhabditis*. The instant specification has not described each of these sequences which minimally contain 8 nucleic acids of SEQ ID NO: 1. Similarly, the specification has not described a representative number of nucleic acids which minimally encode 6 amino acids of SEQ ID NO: 3. The claims are broadly drawn to large numbers of nucleic acids which have been neither described nor contemplated.

With respect to biallelic markers of SEQ ID NO: 1, the art teaches that SNP, biallelic markers, occur approximately every 100-300 bases. Thus it would be expected that in the instant 81,000 base pair nucleic acid, approximately 270-810 would be present. The six biallelic alleles which have been described in the instant specification are not representative of the entire genus of nucleic acids which are encompassed by the instant claims. Since the specification has not described how one would determine whether the nucleic acid which minimally contains 8 nucleotides from SEQ ID NO: 1 is an AA4RP-related biallelic nucleic acid, the claim has been broadly read to encompass any nucleic acid which minimally contains 8 nucleotides from SEQ ID NO: 1. The

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nucleic acids described in the specification as biallelic markers are not representative of the entire genus and therefore, at the time the invention was made, applicant was not in possession of a representative number of members within the genus.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’ required a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”. In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described. Since the specification neither describes a representative number of nucleic acids which minimally contain 8 nucleotides from SEQ ID NO: 1, nor a representative number of biallelic

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markers from SEQ ID NO: 1, applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Armentano et al. (US Pat. 5,877,011, March 2, 1999).

Armentano et al. (herein referred to as Armentano) teaches an isolated, purified or recombinant polynucleotide comprising 14 matches of SEQ ID NO: wherein the continuous nucleotides comprise a T at position 12347. SEQ ID NO: 1 of Armentano, nucleotides 21156-21169 are 100% identical with nucleotides 12345-12358 of SEQ ID NO: 1. Thus, the nucleic acid of Armentano comprises at least one of the nucleotide positions of SEQ ID NO: 1, namely 12347 and comprises at least 12 contiguous nucleotides, namely 14 contiguous nucleotides (see alignment). Armentano teaches vectors and host cells comprising the Ad 17 nucleic acid of SEQ ID NO: 1. Therefore, since Armentano teaches every limitation of the claimed invention Armentano anticipates the claims.

11. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Waters et al. (Genbank Accession Number AF086808, October 1998).

Waters et al. (herein referred to as Waters) teaches a nucleic acid from *bos Taurus* fertilin beta mRNA (ADAM 2). The nucleic acid comprises 16 contiguous nucleotides of SEQ ID NO: 1. Waters teaches a nucleic acid in which nucleotides 1801-1786 are 100% identical with nucleotides 12338-15353 of SEQ ID NO: 1. The nucleic acid comprises a T at position 12347 of SEQ ID NO: 1. Thus, since Waters teaches every limitation of the claims, Waters anticipates the claimed invention.

12. Claims 1-2, 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Hattori et al. (Genbank Accession Number AP001480, May 2000).

Hattori et al. (herein referred to as Hattori) teaches a nucleic acid clone from chromosome 11q which contains at least 121 contiguous nucleotides from SEQ ID NO: 1 including position 12347. A search was performed for nucleotides 12280-12400 of SEQ ID NO: 1 and the nucleic acid taught by Hattori is 100% identical with SEQ ID NO: 1 including a T at position 12347. Nucleotides 55154-55034 of Hattori are 100% complementary to SEQ ID NO: 1, positions 12280-12400. Moreover, Hattori teaches a 312 base pair nucleic acid encoding amino acid SEQ ID NO: 3. Therefore, the nucleic acid taught by Hattori anticipates the claims.

13. Claim 15 is rejected under 35 U.S.C. 102(a) as being anticipated by Chamuleau et al. (WO 00/03013, January 20, 2000).

Chamuleau teaches a nucleic acid sequence which encodes 366 amino acids of SEQ ID NO: 3. Specifically, nucleotides 10-1107 encode all 366 amino acids of SEQ ID NO: 3. Therefore, the nucleic acid of Chamuleau anticipates the claimed invention.

14. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al. (Genbank Accession Number AI528320, March 1999).

Marra et al. (herein referred to as Marra) teaches a nucleic acid from mouse similar to Apolipoprotein A-IV precursor which encodes 26 amino acids of SEQ ID NO: 3. Nucleotides 443-520 of the nucleic acid taught by Marra encode amino acids 144-169 of SEQ ID NO: 3. Thus, since Marra has taught every limitation of the instant claim, Marra anticipates the claimed invention.

15. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Shaikh et al (Genbank Accession Number AC007707, August 1997).

As provided in the specification, Genbank Accession No. 007707 contains a partial genomic sequence from chromosome 11. The RPCI11 library was first available in August 1997, as per the attached e-mail.

The nucleic acid taught by Shaikh is 100% identical to an encoded protein of amino acids 55-366 of SEQ ID NO: 3. Thus, positions 76729-75794 of Shaikh encode amino acids 55-366 of SEQ ID NO: 3.

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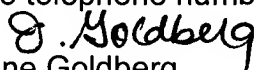
Conclusion


16. No claims allowable over the art.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Jeanine Goldberg
January 27, 2003


B. J. KOBAYASHI
32.001/20000000